

Pertuzumab, Trastuzumab and DOCETaxel Therapy - 21 day cycle

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Pertuzumab is indicated in combination with trastuzumab and DOCETaxel in adult patients with HER2- positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti- HER2 therapy or chemotherapy for their metastatic disease.	C50	00204a	Pertuzumab-ODMS DOCETaxel-N/A Trastuzumab-N/A

* This applies to post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment is administered every 21 days in responding patients until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Cycle 1: Pertuzumab and trastuzumab loading doses

Admin Order.	Day	Drug	Dose	Route	Diluent & Rate
1 or 2	1	Pertuzumab	840mg	IV infusion Observe for 1 hour post infusion	250mL NaCl 0.9% over 60 minutes
2 or 1	1	Trastuzumab	8mg/kg	IV infusion Observe post infusion ^a	250mL NaCl 0.9% over 90 minutes
3	1	DOCETaxel ^b	75mg/m ²	IV infusion	250mL NaCl 0.9% over 60minutes ^c
^a Recommended observation period: Patients should be observed for at least six hours after the start of the first infusion and for two hours after the start of the subsequent infusions for symptoms like fever and chills or other infusion-related symptoms. Any deviation should be noted in local policies.					
^b Primary prophylaxis with G-CSF should be considered to reduce the risk of neutropenic complications (See Adverse Effects/Regimen Specific Complications)					
^c 75-185mg dose use 250mL infusion bag. For doses > 185mg use 500mL infusion bag Use non-PVC infusion bag.					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

NCCP Regimen: Pertuzumab Trastuzumab and DOCETaxel Therapy– 21 day cycle	Published: 30/05/2015 Review: 10/11/2030	Version number: 11
Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 1 of 7
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Cycles 2 and subsequent cycles

Admin Order.	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1 or 2	1	Pertuzumab	420mg	IV infusion Observe for 30-60 minutes post infusion ^c	250mL NaCl 0.9% over 30 minutes if no adverse reactions ^d	Every 21 days
2 or 1	1	Trastuzumab	6mg/kg	IV infusion Observe post infusion ^a	250mL NaCl 0.9% over 30 minutes	Every 21 days
3	1	DOCEtaxel	^e 75mg/m ²	IV infusion	250mL NaCl 0.9% over 60 minutes ^b	Every 21 days for a minimum of 6 cycles
^a Recommended observation period: Patients should be observed for at least six hours after the start of the first infusion and for two hours after the start of the subsequent infusions for symptoms like fever and chills or other infusion-related symptoms. Any deviation should be noted in local policies.						
^b 75-185mg dose use 250mL infusion bag. For doses > 185mg use 500mL infusion bag Use non-PVC infusion bag.						
^c Observation period not required after 3 consecutive treatments with pertuzumab with no reaction.						
^d The infusion time of 30-60 minutes may be used at the discretion of the prescribing consultant.						
^e The dose of DOCEtaxel may be escalated to 100 mg/m ² on subsequent cycles if the initial dose is well tolerated.						
Trastuzumab is incompatible with Glucose 5%.						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indications as above
- HER2 overexpression or HER 2 gene amplification as determined by an accurate and validated assay -Please see *Recommendations on Reporting on HER2 Status in Breast Cancer Patients Available on the NCCP website*.
- ECOG status 0-2
- Patients should have a pre-treatment LVEF ≥ 50%
- Adequate organ function

CAUTION:

- Clinically significant cardiac disease (history of symptomatic ventricular arrhythmias, congestive heart failure or myocardial infarction within previous 12 months)

EXCLUSIONS:

- Hypersensitivity to pertuzumab, trastuzumab, DOCEtaxel, or any of the excipients
- Patients experiencing dyspnoea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of a fatal infusion reaction with trastuzumab
- Significant hepatic dysfunction, contraindicating DOCEtaxel
- Baseline neutrophil count < 1.0 x 10⁹/L
- Pregnancy
- Breastfeeding

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Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 2 of 7

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PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Cardiac function (LVEF using ECHO or MUGA scan)

Regular tests:

- FBC, renal and liver profile before each cycle
- MUGA scan or echocardiogram every 12 weeks during treatment with trastuzumab and at completion of therapy. Where there are signs of cardiac impairment four to eight weekly checks may be more appropriate

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- **Pertuzumab and trastuzumab**
 - None usually recommended. Doses are held or discontinued if unacceptable toxicity occurs. Please see Table 1 below for recommendations on resuming dosing with pertuzumab and trastuzumab after a dose delay or missed doses.
 - Discontinue pertuzumab if trastuzumab is discontinued.
 - Patient may continue to receive both pertuzumab and trastuzumab if DOCetaxel is discontinued due to toxicity or after 6-8 cycles and without evidence of disease progression.

Table 1: Dose modifications of pertuzumab and trastuzumab for delayed or missed doses

Time between two sequential infusions	Pertuzumab	Trastuzumab
<6 weeks	The 420mg dose of pertuzumab should be administered as soon as possible. Do not wait until the next planned dose. Thereafter, revert to the original planned schedule.	The 6mg/kg dose of trastuzumab IV should be administered as soon as possible. Do not wait until the next planned dose. Thereafter, revert to the original planned schedule.
≥6 weeks	The 840mg loading dose of pertuzumab should be re-administered as a 60 min infusion, followed by a maintenance dose of 420mg IV administered every 3 weeks thereafter.	The loading dose of 8mg/kg of trastuzumab IV should be re-administered over approximately 90 min, followed by a maintenance dose of 6mg/kg IV administered every 3 weeks thereafter.

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Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 3 of 7

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Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Drug	Renal Impairment	Hepatic Impairment
Pertuzumab	No dose adjustment is needed. Haemodialysis: no need of dose adjustment is expected.	No need of dose adjustment is expected.
Trastuzumab	No dose reduction required.	No need of dose adjustment is expected.
DOCEtaxel	No dose reduction required.	See Table 2 below.
Pertuzumab (renal and hepatic – Giraud et al 2023) Trastuzumab (renal and hepatic – Giraud et al 2023) DOCEtaxel (renal and hepatic – Giraud et al 2023)		

Table 3: Dose modification of DOCEtaxel in hepatic impairment

Alkaline Phosphatase		AST and/or ALT		Serum Bilirubin	Dose
> 2.5-5 x ULN	and	> 1.5-5 x ULN	and	Normal	Consider 75% of the original dose
<6 x ULN	and/or	> 5-10 x ULN (AST and ALT)	and/or	≤ 1-1.5 x ULN	Consider 50% of the original dose
>6 x ULN	or	>10 x ULN (AST and ALT)	or	>1.5 x ULN	Not recommended

Management of adverse events:

Table 4: Dose modification schedule based on adverse events

Adverse reactions	Recommended dose modification
<ul style="list-style-type: none"> LVEF drops ≥ 10 ejection fraction points from baseline and to below 50% 	Withhold treatment with pertuzumab and trastuzumab. Repeat LVEF within 3 weeks. No improvement or further decline, consider discontinuation. Discuss with consultant and consider referral to cardiology.
Symptomatic heart failure	Discontinue
NCI-CTCAE Grade 4 hypersensitivity reactions	Discontinue
Grade >2 peripheral neuropathy	Decrease dose of DOCEtaxel to 60mg/m ² . If the patient continues to experience these reactions at 60 mg/m ² , treatment with DOCEtaxel should be discontinued.
Grade 3 skin reaction	Discuss with consultant
Grade ≥3 stomatitis	DOCEtaxel will be reduced from 75 to 60 mg/m ² .

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Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 4 of 7

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SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting [Available on the NCCP website](#)

Pertuzumab -Minimal (Refer to local policy)

Trastuzumab-Minimal (Refer to local policy)

DOCEtaxel-Low (Refer to local policy)

For information:

Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - [Available on the NCCP website](#)
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - [Available on the NCCP website](#)

PREMEDICATIONS:

- DOCEtaxel:** dexAMETHasone 8 mg PO twice daily for 3 days, starting one day prior to each DOCEtaxel administration unless contraindicated. Patient must receive minimum of 3 doses pre-treatment.
- Consideration may be given, at the discretion of the prescribing consultant, to the use of a single dose of dexAMETHasone 20mg IV immediately before chemotherapy where patients have missed taking the oral premedication dexAMETHasone as recommended by the manufacturer.*
- Trastuzumab and pertuzumab:** Not usually required unless the patient has had previous hypersensitivity. Paracetamol and antihistamine cover should be considered. Patient should be educated about the possibility of delayed infusion-related symptoms

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS:

Reference:

- NCCP Regimen 00203 DOCEtaxel Monotherapy 75mg/m²-21 day cycle**
- NCCP Regimen 00200 Trastuzumab Monotherapy -21 day cycle**
for detailed information on adverse effects/regimen specific complications.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

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Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 5 of 7

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Version	Date	Amendment	Approved By
1	18/02/2014		Prof Bryan Hennessy
2	30/05/2015	Modification of premedication regimen	Prof Maccon Keane
3	23/06/2016	Modification to allow for substitution of PAClitaxel for DOCETaxel where patients are intolerant, have had significant toxicity or are deemed clinically unsuitable for DOCETaxel.	Prof Maccon Keane
4	09/10/2017	Clarified use of G-CSF and updated administration details.	Prof Maccon Keane
5	18/10/2018	Updated order of administration on treatment table	Prof Maccon Keane
6	13/02/2019	Updated recommendation on number of cycles of DOCETaxel	Prof Maccon Keane
7	02/05/2019	Updated trastuzumab and pertuzumab infusion time from cycle 2 onwards. Updated emetogenic potential	Prof Maccon Keane
8	10/11/2020	Reviewed	Prof Maccon Keane

NCCP Regimen: Pertuzumab Trastuzumab and DOCETaxel Therapy– 21 day cycle	Published: 30/05/2015 Review: 10/11/2030	Version number: 11
Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 6 of 7
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9	09/09/2021	Clarification of requirement for non-PVC infusion bag only	Prof Maccon Keane
10	10/08/2023	Updated emetogenic potential of pertuzumab	Prof Maccon Keane
11	07/11/2025	Reviewed. Updated in line with NCCP standard wording. Updated renal and hepatic dose modifications in line with Giraud et al 2023.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

NCCP Regimen: Pertuzumab Trastuzumab and DOCEtaxel Therapy– 21 day cycle	Published: 30/05/2015 Review: 10/11/2030	Version number: 11
Tumour Group: Breast NCCP Regimen Code: 00204	ISMO Contributor: Prof Bryan Hennessy, Prof Maccon Keane	Page 7 of 7

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